Synopsis on the proposed area of research related to Ph.D work

Theoretical studies on the mechanism of metal catalysed functionalization and transformation of organic compounds.

Submitted By

Poulami Pal

Enrolment Id:03333331708

Registration No. : VB-398 of 2005-06

Under supervission of *Dr. GOURAB KANTI DAS*

Department of Chemistry , Siksha-Bhavana , Visva-Bharati

Santiniketan – 731235 , West-Bengal , India

Synopsis of proposed Ph.D work

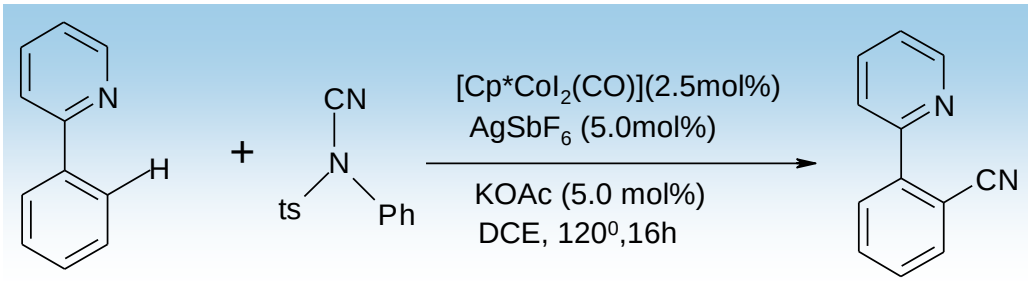
Title – ***Theoretical studies on the mechanism of metal catalysed functionalization and transformation of organic compounds.***

Origin of the research problem

Theoretical and experimental chemists will be able to perform their research work more efficiently if they have model for understanding the chemistry.The cyano group may be considered as one of the most useful functional groups in organic synthesis and can be easily transformed into substituted amines,ketones or aldehydes.The most common procedures for the synthesis of aryl nitriles rely on classical approaches,including the Sandmeyer or the Rosenmund-von Braun reactions. But these transformations have limitations such as the use of (super) stoichiometric amounts of mostly toxic metal cyanidesand harsh reaction conditions. Under transition metal-catalyzed condition, C-H bond functionalization has emerged as a powereful synthetic methodology[1] in present decade. Such processes do not require preactivated substrates such as haloarenes or stoichiometric amount of organometallic reagents and thus serves as an increasingly viable alternative to other traditional processes. Tremendous efforts have been focused on these reactions over the last several years, leading to a variety of transition metal catalyzed direct C-H arylations, alkylations, cyanations and redox-neutral direct alkenylations process[2] of heteroarenes and arenes. Mild reaction condition in such reaction reveals a promosing application in synthesis of various phermaceuticals, natural products, agrochemicals, polymers and feedstock commodity chemicals.[3] Thus far, methods for direct C-H functionalization have mostly been achieved with rather costly, largely exploiting chelation assistance.[4] Recent few years have witnessed the emergence of homogeneous catalysts based on naturally abundant, environmentally benign first row transition metals.[5] Hence, cobalt complexes have specially been identified as increasingly viable catalysts for C-H activation reactions[6], with considerable progress being accomplished with high-valent cobalt complexes, as reported by Kanai/Matsunaga[7] and Akermann[8] and others.

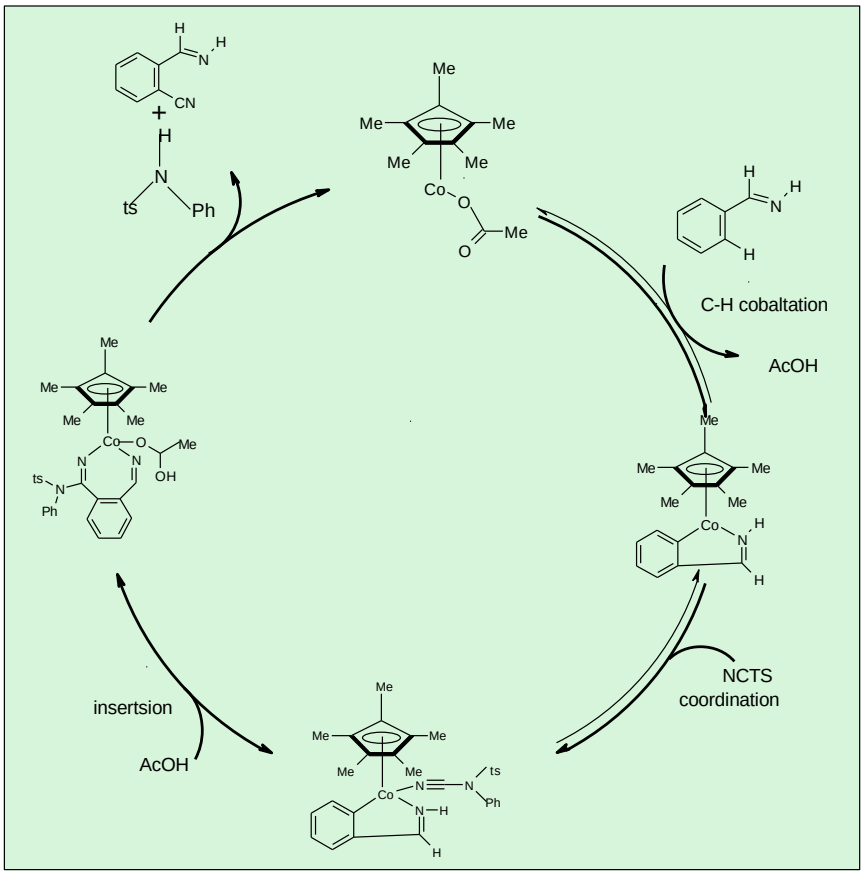
. Considering the practical importance of aryl cyanides, Jie Li and Lutz Ackermann[9] were attracted to devising reaction conditions for for the first cobalt-catalyzed C-H cyanations with the readily available N-cyano-N-phenyl-*p*-toluenesulfonamide (NCTS). In this context it is note-worthy that the direct cyanations with NCTS have thus far only been accomplished with significantly more expensive rhodium or ruthenium catalysts. But Li and Ackermann reported on unprecedented cobalt-catalyzed C-H cyanations which are which are accomplished through carboxylate assistance, and provide expedient access to diversely decorated benzonitriles with ample scope (scheme 1).

Initial experiments indicated [Cp*CoI_2(CO)]to be an efficient catalyst in presence of cocatalytic amounts of $AgSbF_6$ and NaOAc , while other cobalt sources were found to be less effective. These results are indicative of the in situ generation of cationic cobalt(III) acetate catalysts.



Scheme 1

Based on their mechanistic study they proposed a possible catalytic cycle to initiate by a reversible C-H metalation, thus yielding the cyclometalated complex(scheme 2). Subsequent coordination and insertsion of NCTS furnish two key intermediate. Finally, β elimination provide the desired product, while the proto-demetalation regenerates the catalytically active cobalt(III) carboxylate catalyst.



Scheme 2

Our present interest is to investigate the mechanism of C-H cyanation on arene using NCTS catalysed by cobalt(III)acetae in details and reveal the activation energy, stereoselectivity as well as the rate determining step of the reaction.

In addition to the above plan our next attention is on the reaction mechanism of organic transformation of the Pt-metal catalyzed reactions. Literature survey reveals that the propargylic ester derivatives undergo several useful transformations under the catalytic action of platinum-salt.

Objectives of the work :

(a) To collect all the plausible mechanisms of action of homogeneous Co-salt and Pt-salt.
(b) To identify the stationary points involved in the pathway of the plausible mechanisms.
(c) To compare the local and global activation energy involved in each mechanisms. From this data rate determining step of the mechanism will be determined.
(d) To identify the most favorable pathway of the reaction.
(e) To study the effect of substrate variation on the reaction.
(f) To predict the outcomes of other unknown reactions.

Methodology : *Computational Method*

Methods of calculations

For computational modelling of the proposed research work, Quantum Mechanical (QM) ethods will be adopted. The geometry optimization and energy calculation calculation of all the system will be performed by using Gaussian 09 [10]software. For visualizing the output files, some graphics software like Gauss view[11], molden[12], Gabedit[13] or VMD etc will be used.

For most of the cases we will employed Density Functional Theory (DFT) methods for finding out the stationary points. B3LYP hybride functional ang 6-31G*basis set will be used for this purpose. In most of the cases Cartesian Coordinateswillbe used to optimize the geometry. For optimization of ground state geometry suitable algorithm will be used.

The most important task of this modeling will be the exploration of the potential energy surface (PES) of the molecular assembly involved in the reactions. The potential energy surface is the most complete description of all the conformers, isomers and energetically accessible motions of a molecular system. The most informative stationary points are the minima and the saddle points. Minima on the potential energy surface (PES) correspond to the optimized geometries. The lowest energy minima is called global minima. The transition structures between the reactants and products of a reaction is a saddle point. At the stationary point the surface is parallel to the horizontal line corresponding to one geometric parameter or to the plane corresponding to two geometric parameters or to a hyper plane corresponding to more than two geometric parameters. Hence, the first derivative of the potential energy with respect to each geometric parameter is zero i.e $\partial E/\partial q=0$. However, a minimum is a minimum in all directions, but a saddle point is a maximum along the reaction coordinate amd a minimum all other directions. Thwey can be distinguished by the second derivative of energy with respect to the nuclear coordinates. Mathematically, it can be written as, at the minimum $\partial^2 E/\partial^2 q>0$ for allvalues of q; and at the saddle point, $\partial^2 E/\partial^2 q>0$ for all q, except along the reaction coordinate. Along the reaction coordinate, $\partial^2 E/\partial^2 q<0$. A PES can be used to find both the saddle points and the reaction coordinates.

Year wise plan of work and targets to be achieved:

The first year of the project will be used to explore various Co-catalysed C-metalation and reductive elimination reactions that utilise the Grignard reagent to produce low valent Co-complex as intermediate. Various computational data will also be collected during this period.

The next one year period will be used to study the Co-catalysed concerted metalation deprotonation pathway (CMD) along with other reactions. We will study all these reactions in detail in both gas phase and in solution phase. The potential energy surface will also be explored to find out the mechanistic details and various electrostatic interactions occurring in the transition state.

The last year of the period will be utilised through studying comparative catalytic action of other metals like Au, Pd, Pt etc metals along with the study of Co-catalysed reactions.

Future Prospect :

Considering all the reported experimental results it may be stated that the study of the mechanism of the reaction pathway C-H cyanation on arene catalyzed by high-valent cobalt catalyst in presence of acetic acid reveals us several features of the reaction such as : activation energy,stereoselectivity and the rate determining step of the reaction. We hope that all these works will give successful results. We also believe that the outcome of our theoretical investigation will give a new idea about the C-H cyanation reactions of arenes and heteroarenes.

References :

1. Li, B.-J.; Shi, Z. *J.Chem. Soc. Rev.* **2012,**41,5588
2. Nakao, Y.; Kanyiva, K. S.; Oda,S.; Hiyama, T. *J.Am.Chem.Soc.* **2006,**128,8146
3. Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *Angew. Chem., Int. Ed* **2012,**51, 8960-9009
4. Ano, Y.; Tobisu, M,;Chatani, N. *Org. Lett.* **2012,**14,354-357
5. Yamaguchi, J.; Muto, K.; Itani, K.; *Eur. J. Org. Chem.* **2013,**2013,19-30
6. Ackermann, L.*J. Org. Chem.* **2014,**79,8948-8954
7. Ikemoto, H.; Yoshino, K.; Matsunaga, S.; Kanai, M. *J.Am.Chem.Soc.* **2014,**136,5424-5431
8. Li, J.; Ackermann, L. *Angew. Chem. Int. Ed.* **2015,**54,8551-8554
9. Li, J.; Ackermann, L. *Angew. Chem. Int. Ed.* **2014,** 53,1-5
10. Official Gaussian Website : http://www.gaussian.com
11. Official Gaussian Website : http://www.gaussian.com
12. Schaftennar , G.; Noordik, H., J. *Comput Aided Mol.Des*.,**2000 ,**14,123
13. A.R.Allouche, Official GabeditWebsit :http//gabedit.souceforge.net